Diphtheria
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Diphtheria

Overview [1,2,3,4]

For a more complete overview of Diphtheria, refer to the following texts:

- Control of Communicable Diseases Manual (CCDM)
- Red Book, Report of the Committee on Infectious Diseases.
- "Pink Book", Epidemiology and Prevention of Vaccine-Preventable Diseases
- Manual for the Surveillance of Vaccine-Preventable Disease

Case Definition [4]

Clinical description

An upper-respiratory tract illness characterized by sore throat, low-grade fever, and an adherent membrane of the tonsil(s), pharynx, and/or nose.

Laboratory criteria for diagnosis

- Isolation of *C. diphtheriae* from a clinical specimen.
- Histopathologic diagnosis of diphtheria

Case classification

Probable: A clinically compatible case that is not laboratory confirmed and is not epidemiologically linked to a laboratory-confirmed case.

Confirmed: A clinically compatible case that is either laboratory confirmed or epidemiologically linked to a laboratory-confirmed case.

Comment

Cutaneous diphtheria should not be reported. Respiratory disease caused by nontoxigenic *C. diphtheriae* should be reported as diphtheria. All diphtheria isolates, regardless of association with disease, should be sent to the Diphtheria Laboratory, National Center for Infectious Diseases, CDC. Rarely, respiratory diphtheria may result from infection with other *Corynebacterium* species (C. Ulcerans or C. pseudotuberculosis). These isolates should also be forwarded to the CDC.

Information Needed for Investigation

- **Verify clinical diagnosis.** What laboratory tests were conducted? What were the results? What are the patient's clinical symptoms?
- **Establish the extent of illness.** Does the illness meet the case definition? Is the patient properly vaccinated? Are there others with similar symptoms?
- **Contact the Regional Communicable Disease Coordinator** assigned to your area.
- **Contact the Bureau of Child Care** when case(s} are associated with a child-care facility.

- **Complete the Record for Investigation of Diphtheria** 580-0815 (IMMP-5), which can be accessed through the DHSS Internet site.

Case/Contact Follow-Up And Control Measures

Determine the source of infection.

Immediate action on all highly suspect cases (including cutaneous) is warranted until shown not to be toxigenic *C. diphtheriae.* The following action should also be taken for any toxigenic *C. diphtheria* carriers who are detected.

- Contact the Regional Communicable Disease Coordinator assigned to your area.
- Obtain appropriate cultures and preliminary clinical and epidemiological information including vaccine history.
- Begin early presumptive treatment with antibiotics and antitoxin. Start antibiotics and antitoxin. Impose strict isolation until at least two cultures, collected at least 24 hours after antibiotic treatment ended, are negative.

Control Measures[1,2,3,4]

- Identify close contacts, especially household members and other persons directly exposed to oral secretions of the patient. Culture all close contacts, regardless of their immunization status. Ideally, culture should be from both throat and nasal swabs. After culture, all contacts should receive antibiotic prophylaxis.

  Inadequately immunized contacts should receive DTaP/DT/Td boosters. If fewer than three doses of diphtheria toxoid have been given, or vaccination history is unknown, an immediate dose of diphtheria toxoid should be given and the primary series completed according to the current schedule. If > 5 years have elapsed since administration of diphtheria toxoid-containing vaccine, a booster dose should be given. If the most resent dose was within 5 years, no booster is required. (See the ACIP's 1991 *Diphtheria, Tetanus, and Pertussis: Recommendations for Vaccine Use and Other Preventive Measures* for schedule for children <7 years of age.)

  Unimmunized contacts should start a course of DTaP/DT/Td vaccine and be monitored closely for symptoms of diphtheria for 7 days.

ACIP-Recommended Routine Vaccination Schedule[2,3]

Vaccine	2 Months	4 Months	6 Months	15-18 Months	4 – 6 Years	11 – 18 Years
Diphtheria, Tetanus, Pertussis	Dose 1	Dose 2	Dose 3	Dose 4	Booster	--
DTaP- Hib	--	--	--	Dose 4	--	--
DTaP, Hepatitis B, Polio	Dose 1	Dose 2	Dose 3	--	--	--
Td	--	--	--	--	--	Booster

Refer to the Epidemiology and Prevention of Vaccine-Preventable Diseases (Pink Book) Table 1. Catch-up schedule for children age 4 months through 6 years, and

Table 2. Catch-up schedule for children age 7 through 18 years, for children who are un-immunized or behind on immunizations.

Tetanus and diphtheria toxoids (Td) is recommended at age 11-12 years of age if at least 5 years have elapsed since the last dose of tetanus and diphtheria toxoid-containing vaccine. Td boosters are recommended every 10 years.

Contraindications and precautions to vaccination: [2,3]
Persons with a history of neurologic or severe allergic reaction following a previous dose should not receive additional doses of diphtheria toxoid. Diphtheria toxoid should be deferred for those individuals who have moderate to severe acute illness, but persons with mild illness may be vaccinated. Immunosuppression and pregnancy are not contraindications to diphtheria toxoid.

- Treat any confirmed carrier with adequate course of antibiotic, and repeat cultures at a minimum of 2 weeks to assure eradication of the organism. Persons who continue to harbor the organism after treatment with either penicillin or erythromycin should receive an additional 10-day course of erythromycin and should submit samples for follow-up cultures.
- Treat any contact with antitoxin at the first sign of illness.

General Guidelines For Antimicrobial Therapy:
- Refer to Diphtheria section in the Control of Communicable Diseases Manual (CCDM).
- Refer to Diphtheria section in the Red Book.
- Refer to Diphtheria section in Epidemiology and Prevention of Vaccine-Preventable Diseases (Pink Book).

Laboratory Procedures[3]

Culture of the lesion is done to confirm the diagnosis. It is critical to take a swab of the pharyngeal area, especially any discolored areas, ulcerations, and tonsillar crypts. Culture medium containing tellurite is preferred because it provides a selective advantage for the growth of this organism. A blood agar plate is also inoculated for the detection of hemolytic streptococcus. If diphtheria bacilli are isolated, they must be tested for toxin production.

Gram Stain and Kenyon stain of material from the membrane itself can be helpful when trying to confirm the clinical diagnosis. The Gram stain may show multiple club-shaped forms, which look like Chinese characters. Other *Corynebacterium* species ("diphtheriods") that can normally inhabit the throat may confuse the interpretation of direct stain. However, treatment should be started if clinical diphtheria is suggested, even in the absence of a diagnostic Gram stain.

In the event that prior antibiotic therapy may have impeded a positive culture in a suspect diphtheria case, two sources of evidence may aid in presumptive diagnosis: (1) isolation of the *C. diphtheriae* form culturing of close contacts, and/or (2) a low non-protective diphtheria antibody titer in sera obtained prior to antitoxin administration (<0.1 I.U.) This is done by commercial laboratories and requires several days.

To isolate *C. diphtheriae* for carriers, it is best to inoculate a Löffler's or Pai's slant with the throat swab**.** After an incubation period of 18-24 hours, growth from the slant is used to inoculate a medium containing tellurite.

All *C. diphtheriae* isolates also should be sent through the state health department to the Diphtheria laboratory, national Center for Infectious Diseases of the Centers for Disease Control and Prevention (CDC).

Reporting Requirements

Diphtheria is a Category I disease and shall be reported to the local health authority or to the DHSS within 24 hours of first knowledge or suspicion by telephone, facsimile or other rapid communication.

1. For confirmed and probable cases complete a "Disease Case Report" (CD-1), and a Record of Investigation of Diphtheria (IMMP-5) revised 9-02.
2. Entry of the complete CD-1 into the MOHSIS database negates the need for the paper CD-1 to be forwarded to the Regional Health Office.
3. Send the completed secondary investigation form to the Regional Health Office.
4. All outbreaks or "suspected" outbreaks must be reported as soon as possible (by phone, fax or e-mail) to the Regional Communicable Disease Coordinator. This can be accomplished by completing the Missouri Outbreak Surveillance Report (CD-51).
5. Within 90 days from the conclusion of an outbreak, submit the final outbreak report to the Regional Communicable Disease Coordinator.

References

1. Chin, James, ed. "Diphtheria", Control of Communicable Diseases Manual, 17th edition. Washington, D.C.: American Public Health Association. 2000: 165-170.
2. American Academy of Pediatrics, "Diphtheria". In: Pickering LK ed. 2000 Red Book: Report of the Committee on Infectious Diseases. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2000, 233-234
3. Atkinson, William & Wolfe, Charles, ed. "Diphtheria" Epidemiology and Prevention of Vaccine-Preventable Diseases 7th ed. Centers for Disease Control and Prevention 2002. 39-48.
4. Wharton, Melinda, & Roush, Sandra, ed. "Diphtheria" Manual for the Surveillance of Vaccine-Preventable Diseases 3rd ed. Centers for Disease Control and Prevention 2002 Ch. 1, 1-11.

Other Sources of Information

1. Centers for Disease Control, National Immunization Program, http://www.cdc.gov/nip/ (6 June 2003)
2. Immunization Action Coalition, http://www.immunize.org/ (6 June, 2003)
3. Demirci, Cem S and W Abuhammour, "Diphtheria" eMedicine Journal, July 2 2002, V 3, N 7. http://author.emedicine.com/PED/topic596.htm (6 June 2003)
4. Singh, MK and PZ Saba, "Diphtheria", eMedicine Journal, September 27,2001, V 2, N 9, http://author.emedicine.com/emerg/topic138.htm (6 June 2003)

MISSOURI DEPARTMENT OF HEALTH AND SENIOR SERVICES
OFFICE OF SURVEILLANCE

RECORD OF INVESTIGATION OF DIPHTHERIA

CHECK PRELIMINARY DIAGNOSIS ☐ CLINICAL CASE ☐ CARRIER ☐ SUSPECT			DATE
PATIENT'S NAME			AGE / SEX / RACE
STREET ADDRESS OR RFD	CITY OR TOWN		COUNTY
PREVIOUS ADDRESS (IF SIGNIFICANT)			DATE MOVED
PLACE EMPLOYED OR SCHOOL ATTENDED	OCCUPATION		
DATE OF ONSET	DATE REPORTED	HOW DID YOU FIRST LEARN OF THIS CASE?	DATE
PATIENT HOSPITALIZED? ☐ YES ☐ NO	DATE	ATTENDING PHYSICIAN	
NAME OF HOSPITAL	HOSPITAL PHYSICIAN		

CHIEF CLINICAL SYMPTOMS WITH DATES

TREATMENT (TYPE, AMOUNT, DATES)

BACTERIOLOGICAL RESULTS OF NOSE AND THROAT CULTURES FROM PATIENT

DATE COLLECTED	RESULTS		DATE COLLECTED	RESULTS		NAME OF LABORATORY
	CULTURE	VIRULENCE		CULTURE	VIRULENCE	

RELEASE SPECIMENS

DIPHTHERIA IMMUNIZATION? INOCULATIONS AND DATES		DATE OF BOOSTER
SEVERITY OF DISEASE	WAS ANTITOXIN GIVEN PATIENT?	DATE

(CONTINUED ON REVERSE SIDE)

Are there other associated cases? ☐ Yes ☐ No

If yes, how many, and how associated? _____

_____

_____

_____

Household Sanitation: ☐ Good ☐ Fair ☐ Poor

Milk Supply _____

Other Milk Products _____

Other Pertinent Epidemiological Data: _____

_____

_____

_____

CONTACTS (Household and Other)

NAME AND ADDRESS	AGE	SEX	RELATION TO PATIENT	SIMILAR ILLNESS? ONSET DATE	BACTERIOLOGICAL EXAMINATION		
					DATE	CULTURE	VIRULENCE TEST

NARRATIVE AND FOLLOW-UP NOTES

_____

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_____

PROBABLE SOURCE

☐ RECOVERED ☐ DIED	DATE OF DEATH	CAUSE OF DEATH
INVESTIGATED BY		FINAL DIAGNOSIS
NAME OF AGENCY		DATE